GENERAL NATIONS ABOUT THE PHARMACOLGY OF A. N. S.

Site of action: is the site where there is a problem.

Cellular site of action: is the site of problem and where the drug acts.

This site (where there is infection, pathoconstruction, no release of hormones) is different from another normal site in the body and we call it activated system because the drug will act on this site to change and to produce its effect, so the drug will act on when there is activated system.

To get the drug effect you need activation system, if there is no activation system there will be no drug effect, e.g. pt. with high blood pressure took antihypertensive drug the effect will appear as a decrease in blood pressure (activation system), if pt. with normal blood pressure took antihypertensive drug, there would be no effect, no change in blood pressure (because there is no activation system)

Selective drugs: are drugs which act on specific receptor.
Non-selective drugs: which act on more than one receptor.

Classification of receptors:

1. based on location (adrenergic and cholinergic)
2. based on structure (receptors which have same amino acids in one group, receptors which have ion channels, G protein receptor, receptors having enzymatic action e.g. receptors for steroid hormones such as thyroxin, vitamin D, hydrocortisone or peptide hormones such as insulin or growth hormone)

Receptor organs: are organs targeted by drugs.

Adrenaline, secreted from adrenal gland into the blood stream, acts on organ receptor (indirect effect)

Noradrenaline, secreted from sympathetic system, under activation (direct or local effect on organ)

Systems:

1. Sympathetic system or called adrenergic system because it secretes adrenaline, nor adrenaline and also dopamine. Those three transmitters have same structure called catecholamine.
2. Cholinergic system.

Transmitter bind to ➔ receptors to make ➔ action that produces an effect

So effect is the product of action. Action is the processes that leads to the effect. E.g. Ach binds to M receptor on the heart, induce conformational change (action), leads to relaxation (effect). Another example adrenaline bind to β1 receptors on the heart, induce conformational change (action), lead to tachycardia (effect).

α1 receptors: found on smooth muscles, normally it sends static tones, so when activating these receptors it will lead to vasoconstriction, so the effect in the end is hypertension and decrease perfusion in kidney, this can be treated by giving antagonist or blocker for α1 receptors e.g. prosozine

α2 receptors: also causes vasoconstriction but in less intense than α1, that's why most of the drug are blockers for α1, and found in nerve terminals which at that site(presynaptic neurons) nor adrenaline is released. The activation of α2 receptors leads to decrease nor adrenaline discharge (action).
α2 inhibits, stops, regulates the secretion of nor adrenaline, over activation of α2 lead to more decrease in noradrenaline release, cause shock and hypotension, so pt. with hypertension we give him α2 agonist drug e.g. clomidine and methyldopa(treatment of AHT during pregnancy).

For hypotension, we use α1 agonist drug

septic shock treatment: α1 agonist which is sympathomematic (adrenaline + noradrenalin), α2 antagonist.

Rhinitis: caused due to dilatation, treatment by Naphazoline which causes vasoconstriction

So as conclusion hypertension treatments are:

1) α1 blocker (prosazin),
2) α2 agonist, mainly central (methydopa, esp. in pregnancy), (clomidine),
   α2 agonist drugs are not suitable for D.M. pt. because they will lead to more decrease in insulin release
3) β2 agonists
4) β1 blocker (if the cause was due to increase in cardiac output due to activation of β1 rceptors)

B antagonist (beta-blockers):

1) non-selective drug e.g. propranolol
2) selective drug e.g. atenolol
3) α1 + β blocker e.g. carvedilol
4) partial beta-blocker e.g. pindolol

Note: there is difference between drug effect and class effect, drug effect is more specific.

Effect of β blocker on renal system: (this mechanism is used in treatment of hypertension)

1- β Blocker cause decrease in renin release leads to decrease conversion of angiotensin I to angiotensin II
2- angiotensin II is the potent vasoconstrictive factor

drugs for some diseases:

1. HIT/ asthma, β2 agonist, salbutamol

2. Anaphylactic shock, β2 agonist + adrenaline
3. Arrhythmia, β blocker
4. Anxiety, β blocker, propranolol
5. Migraine, β blocker

Types of antagonism:

1) physical antagonism: e.g. charcoal adsorbs morphine and can prevent their absorption, used in alkaloidal poisoning.
2) Chemical antagonism: two substances or drugs react together and form inactive product. E.g. heparin and protamine, Al(OH)3 and HCl.
3) Physiological antagonism: two drugs act on the same biological system but produce different effects. E.g. insulin and glucagon on glucose level, histamine and adrenaline on bronchial and blood pressure.
4) Pharmacological antagonism: one drug (antagonist) blocks the receptor action of the other (agonist).

Pharmacological action:

1- **Competitive:**
Antagonist is similar to agonist, bind to the same site and length, bind with the receptor of agonist, the desirable maximal response can be attained by increasing the dose of agonist, antagonists has affinity but no intrinsic activity, antagonist binding is reversible and weak and by increasing the dose of agonist we can get the effect (displacement effect), strong binding is irreversible, e.g. morphine.

2- **Uncompetitive:**
Antagonist is not similar to agonist, bind to the other site of recptor, maximal receptors depend only on antagonist concentration, e.g. diazepam.

Partial agonist: has affinity and moderate efficacy, compete with the receptor site, produce submaximal response.

Prolonged exposure:

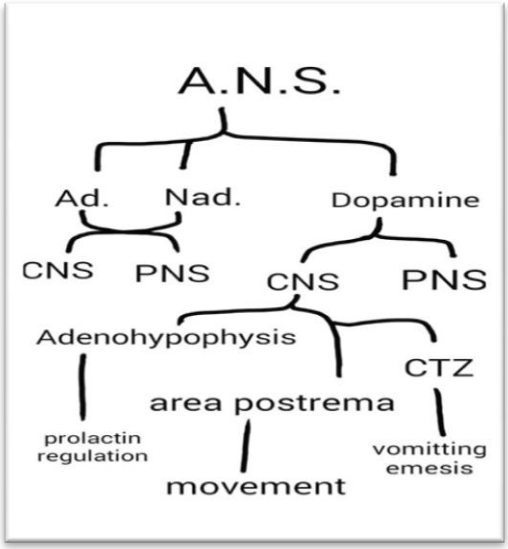
1) Desensitization
2) Down regulation: degeneration of receptors, decrease sensitivity, decrease no. of receptors. Asthmatic pt. becomes irresponsive to Ventolin inhaler due to up regulation.
3) Up regulation: prolonged use of the drug, increase receptor expression. Therefore, βblocker drugs must not be stopped suddenly but gradually.

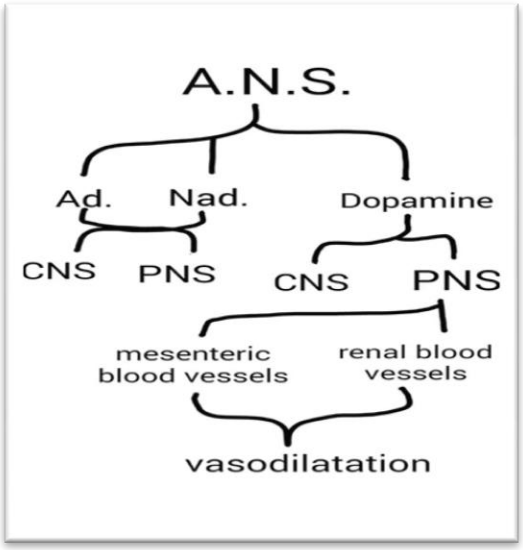
Note: Up means increase the number of receptors.

GENERAL NATIONS ABOUT THE PHARMACOLGY OF A. N. S. 1

Adrenergic system:

1- Main transmitters
2- Adrenergic transmission
3- Drugs that act on adrenergic system





Transmitter of adrenergic system: (adrenalin, noradrenalin, dopamine)

1. Adrenalin and noradrenalin act in the CNS and PNS
2. Dopamine acts on CNS mainly D2 receptor in:
   - *adenohypophysis: inhibition of prolactine
   - *area of pastrium: regulation of movement
   - *CTZ: induce vomiting
   - Also dopamine acts on PNS: renal and mesenteric vessels

Some drugs:

1. Bromocriptine (dopamine agonist) non selective is used in the treatment of hyperprolactinema
2. levodopa (dopamine agonist) is used for Parkinson disease which occurs as result of absent of dopamine
3. promathazine (antagonist) used to stop vomiting

Side effects of promethazine:

1) Act on the desirable cells, but also have non-desirable effects on other cells.
2) Anti-vomiting (desirable effect)
3) Hyperprolactinemia
4) Movement disturbance

Note: so drugs may have more than one effect some are desirable other are not depending on the case of the patient

Dopamine dosage:

Pharmacological classification:

- Low dose 1 – 5 mg/kg/min. acts on D receptors
- Moderate dose 5 – 10 mg/kg/min. acts on β1 receptor
- High dose > 10 mg/kg/min. acts on α1 receptors

Clinical classification:

- Low dose 1- 10 mg/kg/min.
- High dose > 10 mg/kg/min.

Notes:

1. drugs which have pharmacological effect may not have clinical effect because they do not benefit the patient but those who have clinical effect have pharmacological effect
2. Dopamine is not given orally or by injections because of degradation by enzymes but it is preferred to be taken as drops

Cardiogenic shock: condition of bradycardia and hypotension. Dopamine is used in pt. with cardiogenic shock or septic shock because it causes increase in blood pressure and urine outflow.

How to determine the dopamine dosage?

200 mg (ampule of dopamine) + in 500 ml (of dextrose)

= 200 mg/ 500ml = 2 mg/ 5 ml = 2000 µg/ 5 ml = 400 µg/ml (400 µg of dopamine in each 1 ml of dextrose)

Choose the dose that suits the pt.'s case. Suppose its 6µg/ min. and pt. weight is 70 kg, so

70 kg X 6 µg/min. = 420 µg/min. (and the standard is 400µg/ ml) so we give the pt. 1 ml/ min.

(each ml = 20 drops) so we give him 20 drops/min.

Adrenergic transmission:

Means that how the transmitter is release from pre neuron transmitted to synaptic cleft and then to post neuron

1) Biosynthesis of transmitter: ex: thyrosin to dopa to dopamine
2) Storage in vesicles
3) Releasing to synaptic cleft
4) Interaction with receptors and response
5) Inactivation: meaning that after the transmitter done its action it undergoes degradation and release
    - Active or uptake mechanism: Uptake 1 (carrier protein binds, transmits and returns it to the same neuron, and is degraded inside it by enzyme MAO, monoaminooxidase, this enzyme degrades adrenaline, noradrenaline, dopamine and autocoids). Uptake 2 (uptake to another neuron or tissue and degraded by COMPT)
    - Simple diffusion
    - Enzymatic inactivation

Drugs that block uptake 1:

presynaptic and post synaptic acting drugs e.g. presynaptic, tyramine increases the release of adrenaline from presynaptic.

Cocaine, uptake 1 blocker: acts on post synaptic cleft, blocks uptake1 so increases the action of adrenergic system and all its side effects.

MAO inhibitors, as a treatment of psychological people (schizophrenia) increase the concentration in nerve endings and storage form so increase release and increase the effect more than cocaine.

SHARE & CARE 39

الملخص مأخوذ من عمل الطالبة مريم خالد وتم اضافة ملاحظات بسيطه اليه بأشراف اعضاء SHARE ونبقى بشر نصيب ونخطا، ان اصبنا فمن الله وان اخطانا فمن انفسنا ومن الشيطان
الملخص ليس له اي علاقة مباشرة بالهيئة التعليمية

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